Lost in Translation: Participation in Cancer Clinical Trials for Patients With Limited English Proficiency

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Cancer clinical trials are a critical and necessary step for advancing new treatments for patients with cancer, but research has shown that few adults with cancer actually participate in treatment trials. Historically, estimates of trial participation for adults with cancer from the 1990s and early 2000s have been <5%[1]; however, these estimates were based on enrollment to federally sponsored trials. More contemporary estimates that incorporated the contributions of patients to pharmaceutical company–sponsored trials suggest the rate is between 6% and 8%.[2,3] Regardless, the rates remain low, with adverse consequences for the development of new cancer therapies due to trials that are slow to complete or never reach enrollment goals.

In this context, research with the aim of improving the understanding of barriers to trial participation and disparities in access to trials is essential, because the very conduct of trials depends on the availability and willingness of patients to participate. Yet, patients infrequently have an opportunity to participate in trials. According to a recent meta-analysis, trials are available at patients' local institutions only approximately 50% of the time.[3] Even if a trial is available, another 25% of patients are clinically ineligible.[3] Thus, only about 1 in 4 patients even have a chance to discuss trial participation with their physician, despite the fact that patients commonly express a willingness to participate in trials.[4] Indeed, in a recent study, when patients were offered the opportunity to participate in a trial that was available and for which they were clinically eligible, they agreed to do so at astounding rates; >50% of patients of all racial and ethnic backgrounds indicated they wished to enroll.[5]

With this as background, the findings from Jorge et al,[6] reported elsewhere in this issue, represent an important contribution to the literature. The authors investigated the role of limited English proficiency (LEP) as a reason for nonparticipation in clinical trials. Although LEP has been previously examined as a barrier to healthcare in general and to clinical trials in other diseases, little to no research has characterized its role in limiting access to oncology clinical trials. In a retrospective cohort study based on reviews of electronic health record data from 2,793 patients with gynecologic cancers, the authors found a 71% reduction in likelihood of trial participation for those with LEP (2.2% participation) compared with fluent English speakers (7.5%).[6] This finding was robust to covariate adjustment for known confounders of ethnicity and insurance, and the observed trends were consistent across levels of demographic, socioeconomic, and other key variables, further supporting the idea that LEP is independently related to trial participation. Importantly, to underscore the causal relationship, the authors also surveyed gynecologic research staff and providers, who indicated that the main reasons for limited participation of patients with LEP were unavailability of translated consent forms and increased time needed to enroll patients.

A limitation in English proficiency is a modifiable factor that can be easily and readily alleviated as a reason for nonparticipation. Jorge et al[6] suggest several

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strategies. Among these, they noted that up to 20% of trials published on ClinicalTrials.gov list English proficiency among eligibility criteria.[7] In oncology in particular, however, these rates were lower, and in trials that do require English proficiency, it was likely due to a need for patients to participate in an accompanying substudy with patient-facing questionnaires, such as for quality-of-life assessment, rather than for the clinical study itself.

Quality-of-life studies associated with cancer treatment trials are increasingly used to provide patient perspective on the treatment experience. These necessarily rely on use of appropriately validated instruments, some of which will not have been translated beyond English. If so, participation in a quality-of-life ancillary study should never be an exclusion criterion for the associated clinical treatment trial; rather, eligibility should always be worded such that patients who cannot participate in the quality-of-life study may still participate in the clinical component of the trial. The need to enable access to patients of any language in all of the components of a cancer treatment trial has recently propelled the National Cancer Institute to provide translations of commonly used patient symptom-reporting mechanisms, such as the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE).[8]

Jorge et al[6] discuss 2 other limitations in access to trials for individuals with LEP. First, consent forms are not always available in the language in which patients are most proficient. This limitation intersects with another challenging, and endemic, issue in the conduct of trials—that is, the limited resources, time, and effort that physicians and staff have to participate in trials. This issue is especially pervasive in community-based programs, where the conduct of trials is even more challenging but where most patients receive their care.[9] Ultimately, the provision of translated instruments and consent forms and the provision of sufficient resources to sites to enable the time and effort to enroll patients with LEP to trials demands substantial means. Trial sponsors must determine that the need to commit resources toward these ends is sufficient and act on that determination.

Patients with LEP are more likely than those proficient in English to reflect groups who have commonly been underrepresented in clinical research. Thus, a commitment to improve participation in trials for patients with LEP would provide access to the newest treatments for more vulnerable populations. Moreover, it would help to alleviate disparities in trial participation in terms of factors such as race and income. A recent landmark study by Loree et al[10] examining how often Black patients participate in clinical trials that lead to new FDA oncology drug approvals found that only 3.1% of all trial participants were Black compared with an expected rate of 14.1% in a similar set of cancers. Notably, nearly all of the trials included in the dataset (97%) were sponsored by pharmaceutical companies, which predominantly conduct trials in large academic centers and are able to commit substantial resources toward patient enrollment. The results reported by Jorge et al[6] suggest that one strategy whereby pharmaceutical company–sponsored trials may yield improved representation would be to ensure that sufficient support is provided to aide patients with LEP with all patient-facing questionnaires, including consent forms, and to provide translation services as needed.

Patients of any background should have access to the newest treatments in cancer clinical trials without undue barriers. Although recent research has highlighted the outsized adverse impacts of structural and clinical barriers in preventing patients from participating in trials, the investigation of patient-oriented barriers remains a vital concern, because patients who are actually offered a trial are those with the most imminent opportunity to participate. Thus, by addressing the barriers to clinical trial access for patients with LEP, we may further advance the ideal of a more demographically and socioeconomically open and inclusive clinical trial system, to the ultimate benefit of all patients with cancer.

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